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Malignant Mesothelioma of the Tunica Vaginalis Testis: A Report of Two Cases and Review of Literature

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Two cases of rare malignant mesothelioma of tunica vaginalis testis are presented. Both cases were advanced on clinical and radiological studies. One patient was treated with surgical excision followed by chemotherapy and radiotherapy and the other patient was treated with surgery and chemotherapy. Despite aggressive therapy both the patients died within 18 months of treatment. Review of the literature with suggested treatment protocol is presented. The response of malignant mesothelioma to chemotherapy and radiotherapy is poor as indicated by both of our cases. Initial aggressive surgery and adjuvant procedures are necessary soon after diagnosis to achieve long-term survival.

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KEY WORDS: **malignant mesothelioma; tunica vaginalis; testis; cisplatin**

INTRODUCTION

Malignant mesothelioma of the tunica vaginalis testis is a rare tumor. Approximately 64 cases have been reported in world literature to date [1]. Various treatment options have been suggested. However, no definite treatment modality has been established. We treated our first case of malignant mesothelioma in 1994 [2] and a second case in 1996. We present both of our cases with their follow-up and suggest a treatment protocol (Fig. 1) after a review of literature.

CASE REPORT

Patient 1

A 69-year-old teacher from central India presented to the local practitioner with a right-sided scrotal swelling that was diagnosed as a hydrocele. During hydrocelectomy, a nodular swelling was found along the testis from which a biopsy was taken. It was reported as a granulosa cell tumor. Five months later he underwent a right high inguinal orchiectomy at another hospital and then was referred to us for further management. Examination revealed induration and nodularity at the operation site. Review of the histopathology slides from the orchiectomy specimen revealed mesothelioma of the tunica vaginalis. The tumor had a biphasic pattern comprising of both epithelial and sarcomatoid components. The neoplastic epithelial cells were arranged in the form of papillae (Fig. 2) and glands. The cells had moderate amount of eosinophilic cytoplasm with vesicular nuclei, prominent nucleolus, and high mitotic rate. The spindle cells were arranged in fascicles and showed moderate cellular pleomorphism. The hemogram, renal and liver function tests, and tumor markers were within normal limits. Contrast-enhanced computed tomography (CECT) showed thickening of the right inguinal cord but no evidence of retroperitoneal lymphadenopathy. Right hemiscrotectomy with excision of the spermatic cord was done. The histopathological examination revealed metastatic malignant mesothelioma. Considering the locally advanced disease, the patient was given two courses of carboplatin.

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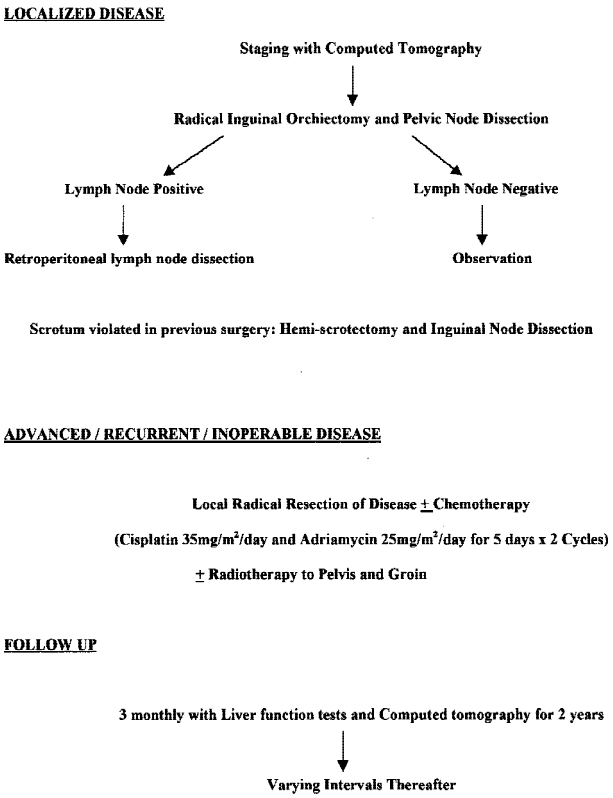

Fig. 1. Suggested treatment protocol for malignant mesothelioma of tunica vaginalis testis.

There was no response to chemotherapy and the patient developed recurrence in the operation scar with contralateral inguinal lymphadenopathy within 1 month. Locoregional radiotherapy (30 Gray in 10 fractions) was given. The patient developed scrotal and penile swelling leading to voiding difficulty, culminating in death due to metastases 3 months after palliative radiotherapy (RT) and 18 months after diagnosis.

Patient 2

A 51-year-old male presented with lower abdominal discomfort, anorexia, and significant weight loss over the past 9 months. He was found to have left testicular swelling by a general practitioner and he had noticed this swelling about 22 years back; the patient was otherwise asymptomatic. Examination revealed a hard and enlarged left testis with normally preserved sensation. There were multiple matted lymph nodes along the left spermatic cord, in the inguinal and the iliac region. Hemogram, liver, and renal function tests and testicular tumor markers (β-human chorionic gonadotropin and α-fetoprotein) were within normal limits. CECT revealed a thick-walled necrotic mass in the left hemiscrotum overlying the testis. There was thickening of the left spermatic cord and

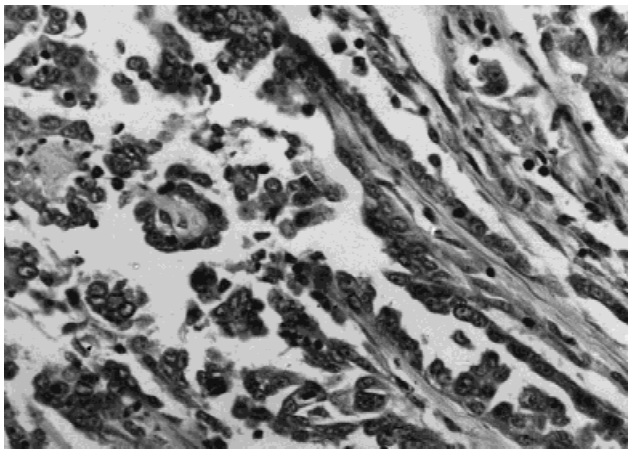

Fig. 2. Photomicrograph showing epithelial component of malignant mesothelioma with papillae formation. The papillae are lined by multilayered cuboidal epithelium (H&E, original magnification ×400).

evidence of diffuse lymphadenopathy in the pelvis and the para-aortic region. The patient underwent a left high inguinal orchiectomy. Intraoperatively, the left testis was 3 × 2 × 2 cm and was displaced to one side by a large necrotic tumor (10 × 6 × 4 cm), to which it was densely adherent.

Histopathological examination revealed malignant mesothelioma of the tunica vaginalis with biphasic pattern. The epithelial component was predominantly tubuloalveolar (Fig. 3), with focal areas showing papillae formation. The cells showed moderate nuclear atypia, high mitotic rate, and abundant eosinophilic cytoplasm. The spindle cell component consisted of spindle-shaped cells arranged in poorly defined fascicles and sheets with nuclei showing marked nuclear pleomorphism and mitosis. The resected margin of the cord showed tumor deposits. In the presence of such advanced disease, the patient was given combination chemotherapy with epirubicin (30 mg/day on day 1, 3, and 5), cisplatin (30 mg /day on days 1–5), and ifosfamide (1 gm/m^2 on days 1–5). Six cycles were given at 3-week intervals. The patient died after the last cycle due to widespread metastases 5 months after diagnosis.

DISCUSSION

Mesothelioma is a relatively rare tumor arising from mesothelial cells lining the pleura, pericardium, and peritoneum. The tunica vaginalis represents an extension of the peritoneal fold during embryonic life and hence is a potential site for the development of malignant mesothelioma. Although Barbera and Rubino [3] have been credited by many as being the first to describe malignant mesothelioma of the tunica vaginalis, the reported case was actually a benign papillary mesothelioma. It was in fact Bailey et al. [4] who in 1955 reported the first case

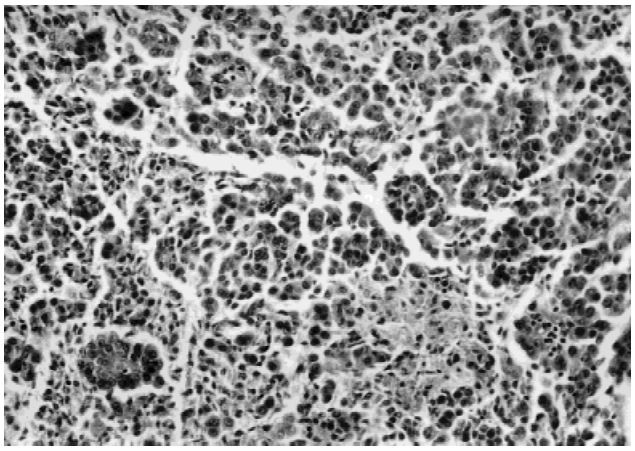

Fig. 3. Malignant mesothelioma with sheets of epithelial cells showing gland formation and areas of necrosis (H&E, original magnification ×200).

of malignant mesothelioma of the tunica vaginalis. Carp et al. [5] reviewed 37 cases reported till 1990 and a total of 64 cases have been reported to date [1].

Most cases of mesothelioma of the tunica vaginalis are malignant, similar to those seen in the peritoneal cavity. In fact it represents the most common primary malignant tumor of the tunica vaginalis. Malignant mesotheliomas are classified into three histological types, epithelial, sarcomatoid, and biphasic. Epithelial mesotheliomas may be papillary, glandular (tubuloalveolar), or solid [6]. Sarcomatoid mesotheliomas consist of poorly defined fascicles of spindle cells. Biphasic mesotheliomas show both epithelial and fibrous patterns. The neoplastic cells of the epithelial component are typically cuboidal with oval, vesicular nuclei and moderate amounts of eosinophilic cytoplasm. Significant nuclear atypia, prominent nucleoli, and high mitotic rate are commonly observed [6]. Prognosis is not affected by histological pattern.

The differential diagnosis of a malignant mesothelioma includes mesothelial hyperplasia, benign papillary mesothelioma, and metastatic adenocarcinoma. Mesothelial hyperplasia occurs as a common response to acute and chronic inflammation and chronic effusions. The presence of grossly visible nodules, necrosis, nuclear atypia, and deep infiltration favor a diagnosis of malignant mesothelioma over hyperplasia [7,8]. The diagnosis may be facilitated by the use of immunohistochemistry, which shows intense cytoplasmic immunopositivity for epithelial membrane antigen (EMA) in malignant mesothelioma. Benign papillary mesotheliomas are characterized by fibrous papillae lined by a single layer of flattened to cuboidal mesothelial cells that may contain basal vacuoles. The nuclear features are benign and mitotic figures are sparse or absent [9,10]. Malignant mesothelioma should also be differentiated from metastatic adenocarcinoma by ruling out the presence of a primary adenocarcinoma elsewhere and by negative reaction to mucin stains (periodic acid schiff and mucicarmine). Malignant mesotheliomas are cytokeratin and epithelial membrane antigen positive but show negative immunostaining for carcinoembryonic antigen, Leu-M1, B72.3, and Ber EP-4 [11]. Electron microscopy may be of additional help. The cells of the epithelial component of malignant mesothelioma typically posses long and slender villi as opposed to short stubby microvilli seen in adenocarcinoma cells [12].

As in our patients, malignant mesothelioma presents clinically as a swelling of the scrotum, often as a hydrocele. It may locally invade the testis, epididymis, dartos, and skin and may metastasize to regional lymph nodes [13]. Preoperative diagnosis is difficult. To date there is only a single report of a correct diagnosis made preoperatively on basis of cytology of the hydrocele fluid [14].

Asbestos exposure is a well-documented risk factor for pleural and peritoneal mesothelioma and such exposure has been reported in patients with tumors of the tunica vaginalis testis with a latent period of 8 to 40 years [15]. Of the 41 cases reported until 1995, 8 patients had history of exposure to asbestos. However, no attempt was made to obtain information about lung asbestos content at autopsy.

Malignant mesothelioma of all patterns has a poor prognosis. The median survival of patients is 5 months, with a range of 1–22 months. In our cases one patient died within 13 and another within 6 months. Tumors confined to the tunica vaginalis may be completely resected and patient survival has been reported for over 10 years [16]. However, once the tumor metastasizes to lymph nodes, the prognosis appears to be gloomy and it behaves like a tumor of the pleura and peritoneum, which rarely respond to available therapy. Chemotherapy and radiotherapy have been largely unsuccessful in providing long-term palliation. So far doxorubicin and cisplatin have been used widely, but with little success. Mesothelioma even responds poorly to high-dose chemotherapy and radiotherapy. Yanagawa et al. [17] used lymphokine-activated killer (LAK) cells and interleukin 2 (IL-2) in successfully controlling the pleural effusion due to mesothelioma, indicating that malignant mesothelioma is sensitive to the immunotherapeutic approach. However, Robinson et al. [18] have refuted the efficacy of IL-2 and LAK cell therapy. Further studies are necessary to evaluate the efficacy of this treatment protocol against mesothelioma at other sites. Treatment failure is mainly due to local recurrence of disease. The retroperitoneal nodes are the most common sites of metastases. The other sites of metastases include supraclavicular and inguinal lymph nodes, lungs, and occasionally intra-abdominal sites. An initial aggressive surgical approach is necessary to achieve cure. If disease recurs, then radical resection

should be contemplated if feasible. These case reports highlight the need for early detection and innovation of other modalities of treatment that may benefit the patient.

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